Remarks

Applicants respectfully request reconsideration of the rejections set forth in the Office Action mailed May 12, 2004. Claims 60 and 64 have been cancelled herein. Accordingly, claims 31, 50, and 68-77 are pending. Claims 31, 50, and 60, 64, and 68-77 have been rejected.

The comments in the Office Action are now addressed in turn.

Rejections under 35 U.S.C. §112, First Paragraph

Claims 31 and 50

Claims 31 and 50 have been rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. The Office contends that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. The Office maintains that the disclosure does not describe a process for obtaining the claimed compound with a chiral purity of >95%.

In addition, Claims 31 and 50 have been rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement. More specifically, the Office has expressed concerns regarding the phrase "chiral purity of >95%". Applicants respectfully traverse these rejections.

Applicants maintain that the specification provides ample disclosure relating to processes for obtaining compounds with a chiral purity of >95%. For example, the specification states at page 13:

> Optically active (R)- and (S)- isomers may be prepared using chiral synthons or chiral reagents, or resolved using conventional techniques. . . . When desired, the R- and S-isomers may be resolved by methods known to those skilled in the art, for example by formation of diastereoisomeric salts or complexes which may be separated, for example, by crystallisation; via formation of diastereoisomeric derivatives which may be separated, for example, by crystallisation, gas-liquid or liquid chromatography; selective reaction of one enantiomer with an enantiomer-specific reagent, for example enzymatic oxidation or reduction, followed by separation of the modified and unmodified enantiomers; or gas-liquid or liquid chromatography in a chiral environment, for example on a chiral support, such as silica with a bound chiral ligand or in the presence of a chiral solvent. It will be

> appreciated that where the desired enantiomer is converted into another chemical entity by one of the separation procedures described above, a further step may be required to liberate the desired enantiomeric form. Alternatively, specific enantiomer may be synthesized by asymmetric synthesis using optically active reagents, substrates, catalysts or solvents, or by converting on enantiomer to the other by asymmetric transformatio.

Moreover, an example of a synthesis of optically active compounds as claimed herein can be found in Figure 4. Examination of the synthetic route indicates that the chiral center is in the first step through the coupling of a chiral amino acid to an amino benzoic acid. As is well known in the art, amino acids with a high degree of optical purity are readily available. For example, enclosed is a copy of technical information on various activated amino acids that were commercially available form Sigma-Aldrich in 1997. See *Tetrahedron: Asymmetry* 1997, *8(7),* Back Cover. See, also, Advanced Asymmetric Synthesis, G.R. Stephenson, Kluwer Academic Publishers, (1996).

Finally, Applicants have provided experimental results for the synthesis of an intermediate having chiral purity of >95%. See, Example 9. This intermediate can be readily transformed to the claimed compounds by reductive alkylation as shown in Figure 4.

Applicants respectfully maintain that the Examiner's concerns have been addressed and request that the rejection be withdrawn.

Claims 68-71

Claims 68-71 have been rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. The Office contends that the limitation of "halobenzyl" does not have a description in the instant disclosure and that the sole species of "chlorobenzyl" does not adequately support the scope of "halobenzyl". Applicants respectfully disagree and traverse this rejection.

Applicants maintain that one of skill in the art would readily appreciate that "halobenzyl" refers to a benzyl group substituted with halogen. This is consistent with IUPAC nomenclature systems. The specification states on page 12, line 28 that halogen refers to fluorine, chlorine, bromine or iodine. The specification further indicates that fluorine, bromine, and chlorine are

preferred. Moreover, the specification provides examples of R_1 being chlorobenzyl (see, e.g., Figure 3, page 29, 34, and 52).

The court has said that "[t]he generic term halogen comprehends a limited number of species, and ordinarily constitutes a sufficient written description of the common halogen species. . . . In the case of a small and closely related group such as the halogens, the naming of the group should ordinarily be sufficient since nothing of consequence would be added by also naming each of the well known members of the group." *See Bigham v. Godtfredsen*, 857 F.2d 1415, 1417, 8 USPQ2d 1266, 1268 (Fed. Cir. 1988) and M.P.E.P. Section 2138.05.

Applicants respectfully maintain that the species chlorobenzyl adequately supports halobenzyl. Applicants respectfully request that the rejection be withdrawn.

Rejections under 35 U.S.C. §112, Second Paragraph

Claims 31, 50, 60, 64, and 68-77 have been rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Office has expressed specific concern regarding the phrase "substituted" which allegedly renders the claims with indefinite metes and bounds. Applicants respectfully disagree and traverse the rejection.

The MPEP and Federal Circuit case law make it clear that the definiteness of the claim language must be analyzed, not in a vacuum, but in light of: i) the content of the particular application's disclosure; ii) the teachings of the prior art; and iii) the claim interpretation that would be given by one possessing the orderinary level of skill in the art at the time the invention was made. M.P.E.P. §2173.02. See also *In re Marosi,* 218 USPQ 1 (Fed. Cir. 1984); and *W. L. Gore & Associates, Inc. v. Garlock, Inc.,* 220 U.S.P.Q. 303 (Fed. Cir. 1983).

The specification indicates at page 12, lines 18-27 that:

> Substituted alkyl, aryl and heteroaryl refer to alkyl, aryl or heteroaryl wherein H atoms are replaced with alkyl, halogen, hydroxy, alkoxy, alkylenedioxy (e.g. methylenedioxy) fluoroalkyl, carboxy (-COOH), carboalkoxy (i.e. acyloxy RCOO-), carboxyalkyl (-COOR), carboxamido, sulfonamidoalkyl, sulfonamidoaryl, aminocarbonyl,

> benzyloxycarbonylamino (CBZ-amino), cyano, carbonyl, nitro, dialkylamino, alkylamino, amino, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylsulfonamido, arylthio, arylsulfinyl, arylsulfonyl, amidino, phenyl, benzyl, heteroaryl, heterocyclyl, phenoxy, benzyloxy, or heteroaryloxy. For the purposes of the present invention, substituted alkyl also includes oxaalkyl residues, i.e. alkyl residues in which one or more carbons has been replaced by oxygen.

As such, when read in light of the content of the particular application's disclosure, Applicants maintain that the claims are definite. Applicants request that the rejection be withdrawn.

Rejections under 35 U.S.C. §102(e)

Claims 60 and 64 have been rejected as being allegedly anticipated by Schall et al. U.S. 6,559,160. As these claims have been cancelled herein, Applicants maintain that the rejection is moot and respectfully request that the rejection be withdrawn.

Conclusion

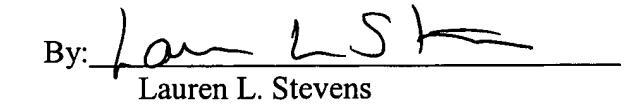
Applicants respectfully maintain that all pending claims are in condition for allowance. Therefore, Applicants respectfully request a Notice of Allowance for this Application from the Examiner. Should any unresolved issues remain, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Please grant any extensions of time required to enter this reply, and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Date: August 5, 2004

By: 

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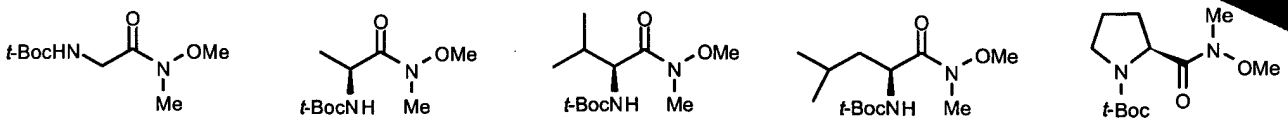

46,512-7	45,845-7	45,846-5	42,383-1	45,885-6

N'-Methoxy-*N*'-methylamides of α-amino acids are useful starting materials for the synthesis of chiral molecules.[1] Addition of nucleophiles gives high yields of ketones; overaddition produces little, if any, alcohols. Reduction of the amides with $LiAlH_4$, DIBAL-H, or Red-Al® produces α-amino aldehydes. Examples in which researchers have utilized these important compounds are shown below.

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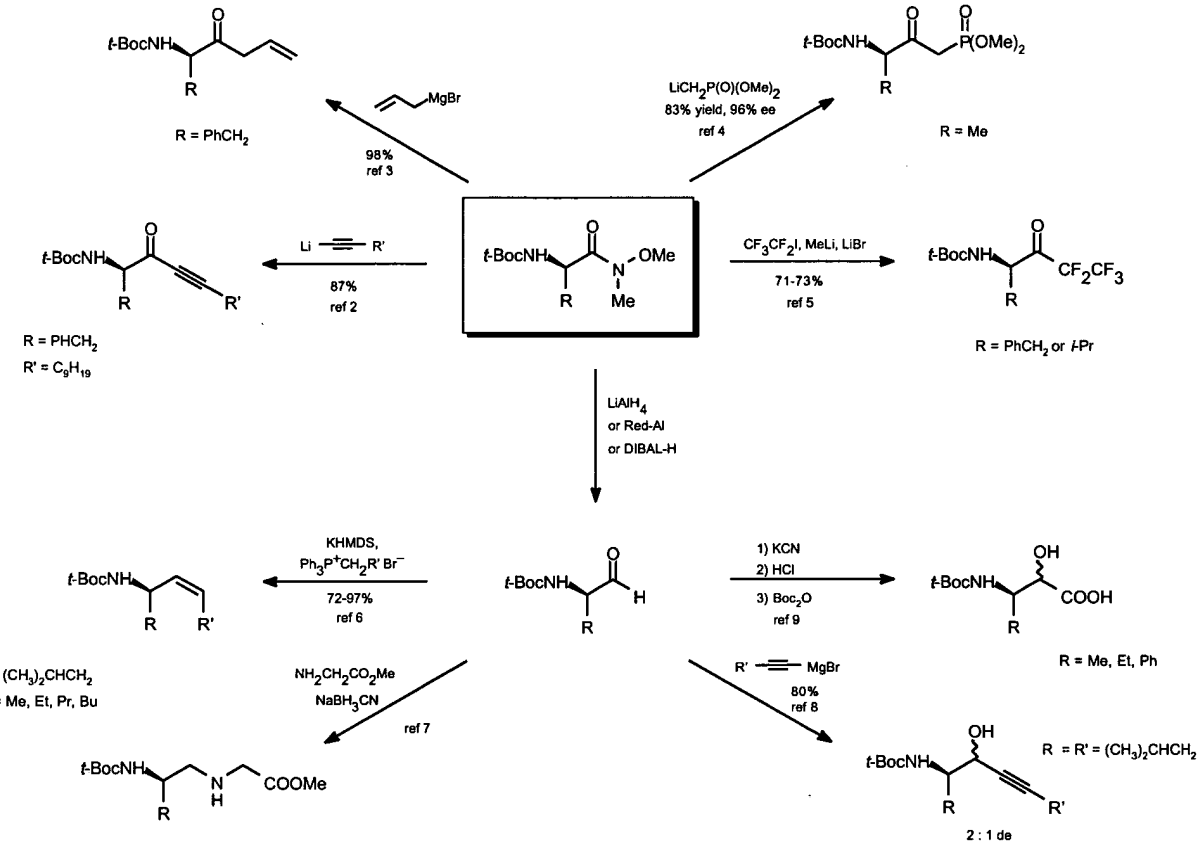

46,512-7 ***N*-(*tert*-Butoxycarbonyl)glycine *N*'-methoxy-*N*'-methylamide,** 98% **1g; 5g**

45,845-7 ***N*-(*tert*-Butoxycarbonyl)-L-alanine *N*'-methoxy-*N*'-methylamide,** 98% **1g; 5g**

45,846-5 ***N*-(*tert*-Butoxycarbonyl)-L-valine *N*'-methoxy-*N*'-methylamide,** 97% **1g; 5g**

42,383-1 ***N*-(*tert*-Butoxycarbonyl)-L-leucine *N*'-methoxy-*N*'-methylamide,** 98% **1g; 5g**

45,885-6 ***N*-(*tert*-Butoxycarbonyl)-L-proline *N*'-methoxy-*N*'-methylamide,** 98% **1g; 5g**

References: (1) Nahm, S.; Weinreb, S.M. *Tetrahedron Lett.* **1981**, *22*, 3815. For a review, see: Sibi, M.P. *Org. Prep. Proc. Intl.* **1993**, *25*, 15. (2) Overhand, M.; Hecht, S.M. *J. Org. Chem.* **1994**, *59*, 4721. (3) Kim, B.M. et al. *Tetrahedron Lett.* **1994**, *35*, 5153. (4) Lucet, D. et al. *Tetrahedron: Asymmetry* **1996**, *7*, 985. (5) Angelastro, M.R. et al. *Tetrahedron Lett.* **1992**, *33*, 3265. (6) Saari, W.S.; Fischer, T.E. *Synthesis* **1990**, 453. (7) Kosynkina, L. et al. *Tetrahedron Lett.* **1994**, *35*, 5173. (8) Bohnstedt, A.C. et al. *Tetrahedron Lett.* **1993**, *34*, 5217. (9) Harbeson, S.L. et al. *J. Med. Chem.* **1994**, *37*, 2918.

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